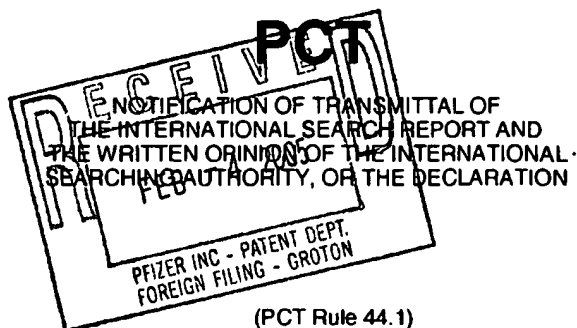


From the INTERNATIONAL SEARCHING AUTHORITY

To:
 PFIZER INC.
 Mailstop 8260-1615
 Attn. Fuller, Grover F.Jr.
 Easter Point Road
 Groton CT 06340
 UNITED STATES OF AMERICA



Date of mailing
 (day/month/year) 31/01/2005

Applicant's or agent's file reference

PC25634A

FOR FURTHER ACTION See paragraphs 1 and 4 below

International application No.

PCT/IB2004/003310

International filing date

(day/month/year) 11/10/2004

Applicant

PFIZER PRODUCTS INC.

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
 1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, within **20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority

 European Patent Office, P.B. 5818 Patentaan 2
 NL-2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Sabine Oblinger

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 48.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference PC25634A	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/IB2004/003310	International filing date (day/month/year) 11/10/2004	(Earliest) Priority Date (day/month/year) 23/10/2003
Applicant PFIZER PRODUCTS INC.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ **Certain claims were found unsearchable** (See Box II).

3. ☒ **Unity of invention is lacking** (see Box III).

4. With regard to the **title**,

the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. 3



as suggested by the applicant.



as selected by this Authority, because the applicant failed to suggest a figure.



as selected by this Authority, because this figure better characterizes the invention.

- b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2004/003310

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
 - a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☒ contained in the international application as filed
 - ☒ filed together with the international application in computer readable form
 - ☐ furnished subsequently to this Authority for the purpose of search
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N1/20 C12Q1/68 A61K39/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, Sequence Search, EMBASE, BIOSIS, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL 'Online! 21 October 2001 (2001-10-21), "Bacteroides sp. 0103 800 partial 16S rRNA gene, strain 0103 800" XP002313696 retrieved from EBI accession no. EM_PRO:BSP416906 Database accession no. AJ416906 the whole document</p> <p>----- -/--</p>	1-3,5,11



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

8 document member of the same patent family

Date of the actual completion of the international search

20 January 2005

Date of mailing of the international search report

31/01/2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Perez, C

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL 'Online! 14 January 2001 (2001-01-14), "Tannerella forsythensis gene for 16S rRNA, strain:TR6." XP002313697 retrieved from EBI accession no. EM_PRO:AB053947 Database accession no. AB053947 the whole document</p> <p>-----</p>	1-3,5,9, 11
X	<p>WO 03/054755 A (HARDHAM JOHN MORGAN ; KRISHNAN RAJENDRA (US); PFIZER PROD INC (US); DR) 3 July 2003 (2003-07-03) page 48, line 30 - page 53, line 24 claims 1-15</p>	1-3,5, 11-29
X	<p>-& DATABASE Geneseq 'Online! 25 March 2004 (2004-03-25), "Porphyromonas gulae 869 16S rRNA DNA." XP002313698 retrieved from EBI accession no. GSN:ADH52847 Database accession no. ADH52847 the whole document</p> <p>-----</p>	1-3,5,11
A	<p>PASTER B J ET AL: "Bacterial diversity in human subgingival plaque" JOURNAL OF BACTERIOLOGY, WASHINGTON, DC, US, vol. 183, no. 12, June 2001 (2001-06), pages 3770-3783, XP002237325 ISSN: 0021-9193 page 3780, left-hand column, paragraph 3 - page 3782, last paragraph</p> <p>-----</p>	1-35
A	<p>WO 99/08691 A (SPACCIAPOLI PETER ; NELSON ERIC (US); PERIODINTIX INC (US); FRIDEN PHI) 25 February 1999 (1999-02-25) page 5, line 19 - page 6, line 6 examples 2-4 claims 1-30</p> <p>-----</p>	1-35

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 5-6, 30-33 completely, 1-4, 11-29 partially

isolated pigmented anaerobic bacterium characterized by a 16S rRNA DNA sequence at least 95 % homologous to SEQ 3, 6, 9, 10 or 13, or a biologically pure culture of said bacteria. An immunogenic composition comprising said bacterium, a vaccine made thereof, and methods for treating, preventing or diagnosing periodontal disease in companion animals

2. claims: 7-8, 34 completely, 1-4, 11-29 partially

same as for invention 1 but with 16S rRNA sequences at least 95 % homologous to SEQ 4.

3. claims: 9-10, 35 completely, and 1-4, 11-29 partially

same as for invention 1 but with 16S rRNA sequences at least 95 % homologous to SEQ 5.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2004/003310

Box II Observations where certain claims were found unsearchable (Continuation of Item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 18 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of Item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB2004/003310

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 03054755	A	03-07-2003	BR 0205775 A	03-08-2004
			WO 03054755 A2	03-07-2003
			US 2003228328 A1	11-12-2003
			US 2005010032 A1	13-01-2005
<hr/>				
WO 9908691	A	25-02-1999	US 6153210 A	28-11-2000
			AU 9017898 A	08-03-1999
			CA 2301065 A1	25-02-1999
			EP 1011693 A1	28-06-2000
			JP 2001515042 T	18-09-2001
			NO 20000688 A	15-03-2000
			WO 9908691 A2	25-02-1999
<hr/>				

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

To:

see form PCT/ISA/220

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/B2004/003310

International filing date (day/month/year)
11.10.2004

Priority date (day/month/year)
23.10.2003

International Patent Classification (IPC) or both national classification and IPC
C12N1/20, C12Q1/68, A61K39/02

Applicant
PFIZER PRODUCTS INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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Authorized Officer

Perez, C

Telephone No. +49 89 2399-2484



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

2007568
International application No.
PCT/IB2004/003310

IAP20 RESULTS INFO 21 FEB 2006

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☒ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☒ in written format
☒ in computer readable form
 - c. time of filing/furnishing:
☒ contained in the international application as filed.
☒ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/IB2004/003310

Box No. II Priority

1. ☒ The following document has not been furnished:

☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. ☐ It has not been possible to consider the validity of the priority claim because a copy of the priority document was not available to the ISA at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

4. Additional observations, if necessary:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/IB2004/003310

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 18 as far as IA is concerned

because:

- ☒ the said international application, or the said claims Nos. 18 as far as IA is concerned relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/IB2004/003310

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	4, 6-8, 10, 30-35
	No: Claims	1-3, 5, 9, 11-29
Inventive step (IS)	Yes: Claims	
	No: Claims	1-35
Industrial applicability (IA)	Yes: Claims	1-17, 19-35
	No: Claims	

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
 INTERNATIONAL SEARCHING
 AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/IB2004/003310

1. Additional remark to item III (no opinion)

Claim 18 is directed to an in vivo therapeutic method, which is considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of said claims (Article 34(4)(a)(i) PCT).

2. Additional remarks to item V (reasoned statement under Rule 66.2(a) (ii) with regard to novelty, inventive step or industrial applicability)

2.1 Present application

The present application is directed to isolated pigmented anaerobic bacterial isolates identified by their 16S rRNA DNA that cause periodontal diseases in companion animals. Said isolates are characterized by comprising a 16S rRNA DNA sequence having at least 95 % or 99 % or 99.5 % homology with a sequence selected from SEQ ID N°3, 4, 5, 6, 9, 10 and 13. In particular three bacterial isolates, a *Bacteroides denticanoris* corresponding to ATCC PTA-5881, a *Porphyromonas levii* corresponding to ATCC PTA-5882 and a *Tannerella forsythensis* corresponding to ATCC PTA-6063 are disclosed. Said isolates are used as immunogenic composition or vaccine for the treatment or prevention of periodontal diseases. Probes consisting of 15 contiguous nucleotides of any of the above sequences are also used as part of a kit for the detection of *Bacteroides*, *Porphyromonas* or *Tannerella* species.

2.2 Prior art documents

The present communication refers to the documents cited in the International Search Report (ISR). Said documents are numbered as in the ISR, i.e. D1 corresponds to the first document cited in the ISR. The numbering will be adhered to in the rest of the procedure.

These prior art documents disclose, among other, the following data:

- (i) **D1** discloses a genomic DNA corresponding to the partial sequence of the 16S rRNA gene of a *Bacteroides* strain, strain 0103 800. Said sequence exhibits high percent identity with all 16S rRNA DNA sequences of the application derived from *Bacteroides denticanoris* strains:
 - it shares 98.7 %, 98.12 %, 98.6 %, 98.6 % and 98.93 % identity with the entire SEQ ID N°3, 6, 9, 10 and 13 of the present application respectively;
 - it exhibits 100 % identity with fragments of said sequences, for example [332-550] of SEQ ID N°3, [145-424] of SEQ ID N°6, [332-565] of SEQ ID N°9, [191-313] of SEQ ID N°10, and [68-179] of SEQ ID N°13.

- (ii) **D2**discloses a genomic DNA corresponding to the sequence of the 16S rRNA gene of a *Tannerella forsythensis* strain TR6. Said sequence exhibits 99.04% identity with the entire SEQ ID N°5 of the present application. Moreover it is 100 % identical with fragment [311-520] of said SEQ ID N°5. Furthermore *Bacteroides forsythus* is provided as a synonym of *Tannerella forsythensis*.
- (iii) **D3** corresponds to an earlier application from the present Applicant already disclosing bacterial isolates identified by their 16S rRNA DNA that cause periodontal disease in companion animals, in particular bacteria from the genus *Porphyromonas*. Many of the 16S rRNA DNA sequences share high percent identity with the sequences of the present application. As an example, the sequence SEQ ID N°89 (ADH52847) corresponding to a 16S rRNA DNA sequence of a *Porphyromonas gulae* strain B69, shares 100 % identity with fragments [69-180] of SEQ ID N°3, [831-942] of SEQ ID N°6, [235-309] of SEQ ID N°4, [32-176] of SEQ ID N°5, [234-302] of SEQ ID N°9, [68-179] of SEQ ID N°10 and [331-565] of SEQ ID N°13. Also disclosed are vaccine composition and kit comprising live or inactivated isolated bacteria, useful for treating or preventing periodontal diseases, as well as hybridization kit for the detection of *Porphyromonas* species (p.48, l.30 - p.53, l.24).
- (iv) **D4** discloses the identification of 275 species or novel phylotypes in human diseased patients, among which many species from the *Bacteroidetes* genus such as *Bacteroides forsythus* and various *Porphyromonas* species. Moreover it refers on page 3780, right column, second paragraph, to a commonly accepted rule for the definition of a bacterial species: a 2 % difference in the 16S RNA DNA sequences is generally used as an indication that the corresponding bacteria belong to different species.
- (v) **D5** reports the treatment of periodontal diseases by administration of metal ions to the site where the microorganisms reside. These ions are microbicidal to the bacterial pathogens such as *B. forsythus* or *P. gingivalis* as shown in example 4, on dogs (see Table 1).

2.3 Statement with regard to novelty and inventive step (Articles 33 (2) and (3) PCT)

2.31 Novelty

The subject-matter of **claims 1-3, 5, 9, 11-29** does not meet the requirements of

Articles 33 (2) and (3) PCT, because said claims lack novelty in view of D1 and/or D2 and/or D3 and their lack of clarity.

- i) Given the wording of the specification, in particular on page 3, lines 1-23, the subject-matter of claim 1 is interpreted as an isolated pigmented anaerobic bacterium "suitable for causing periodontal disease in companion animals" (PCT Guidelines, 11.03.2004, Chapter 5.21-5.23), which is only characterized by the at least 95 % homology of its 16S rRNA DNA sequence to the sequences referred to in claim 1. In other words any isolated pigmented anaerobic bacterium whose 16S rRNA DNA sequence fulfills the conditions set in claim 1, is considered to inherently cause periodontal diseases in companion animals. In this context D1 and D2 disclose 16S RNA sequences of Bacteroides and Tannerella strains which are 98 to 99 % identical to at least one of the whole sequences referred to in claim 1 of D1 and D2 respectively (see § 2.2 i and ii). Such high percentage of identity at the 16S RNA DNA level, less than 2 % difference, is generally recognised as meaning that the 2 corresponding bacteria belong to the same species (see § 2.2 iv). Thus D1 and D2 are prejudicial to novelty of claims 1, 2 and/or 9, because the disclosure, in D1 and D2 respectively, of the 16S rRNA DNA of the Bacteroides species 0103 800 and the Tannerella forsythensis TR6 strain, renders the isolation of said bacterial strains implicit (see PCT Guidelines, 11.03.2004, Chapter 12.04) and the fact that said bacteria are pigmented, anaerobic and suitable for causing periodontal diseases are inherent features of these bacterial species. This lack of novelty also applies to claims 5 and 11 because "Bacteroides denticanoris" is only an arbitrary denomination, and the feature introduced in claim 11 does not restrict the scope of claim 1. Thus D1 and/or D2 anticipate novelty of **claims 1-2, 5, 9 and 11**.
- ii) Moreover it is pointed out that claims 1-3 refer to "a" sequence and not "the whole" sequence selected from SEQ ID N°3, 4, 5, 6, 9, 10 and 13. Since the 16S rRNA DNA sequences provided by D1, D2 and the SEQ ID N°89 of D3 all exhibit 100 % identity to fragments of SEQ ID N°3, 4, 5, 6, 9, 10 and 13 (see § 2.2 i - iii), the bacteria referred to in said documents are prejudicial to novelty of **claims 1-3 and 5, and 11** (see the detailed reasoning above). With regard to D3, this novelty objection further applies to **claims 12-29**, because said document also provides vaccine composition for treating and preventing periodontal diseases as well as hybridization kits for the detection of Porphyromonas species (see § 2.2 iii).

2.32 Inventiveness

The subject-matter of **claims 1-35** does not meet the requirements of Article 33 (3) PCT, because said claims do not involve an inventive step in view of the teachings of D3 in combination with D4 and D5.

D3 is the closest prior art because it already describes vaccines for treating or preventing periodontal diseases in companion animals. The present application differs from D3 by the nature of the bacterial isolates comprised in said vaccine preparation.

Thus the problem to be solved is to provide alternative vaccine for the treatment and prevention of periodontal diseases in companion animals.

However it is clear from the overall literature on periodontal diseases that there are hundreds of bacterial species which are involved in said diseases. For example, D4 reports that 275 species or novel phylotypes were identified in human diseased patients, among which many species from the Bacteroidetes genus such as *Bacteroides forsythus* and various *Porphyromonas* species (see § 2.2 iv). Thus the disclosure of D4 shows that new bacterial isolates involved in periodontal diseases are frequently being identified and that novel bacterial isolates can be expected to be identified in the future. Moreover the results on dogs of D5 confirm that many of these bacterial species are also pathogens for companion animals, for example, *Bacteroides forsythus* (see § 2.2 v).

In this context the skilled person, trying to solve the above problem, would have an incentive to look for new bacterial species and strains, to solve the above problem. In particular the data of D4 and D5 provides a clear incentive to look for new isolates among the species known to be involved in periodontal diseases such as *Tannerella forsythensis* (which is the new designation for *Bacteroides forsythus*, see for example D2) and/or new species among the genera known to be involved in periodontal diseases such as *Porphyromonas*. Thus the present contribution, merely the provision of isolates/species of *Bacteroides denticanoris*, *Porphyromonas levii* and *Tannerella forsythensis*, is a selection among the hundreds of bacterial isolates/strains involved in periodontal diseases in companion animals. In order to be inventive, such a selection must not be arbitrary, but must be justified by the technical purpose, i.e. by a hitherto unknown or unexpected technical effect, caused by those technical features which distinguish the claimed bacterial isolates involved in periodontal diseases from numerous other ones. Due to the absence of any

unexpected function or technical effect of the claimed bacterial isolates, the present selection amounts to nothing more than an arbitrary selection. Consequently, the subject-matter of **claims 1-35**, which is directed to or referred to said bacterium or bacteria culture does not meet the requirements of Article 56 EPC.

2.4 Statement with regard to industrial applicability (Article 33 (4) PCT)

For the assessment of the present **claim 18** on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Additional remarks concerning support of the claimed matter (Articles 5 and 6 PCT)

A) Overall lack of clarity

The claims on file refer to a percent homology. However, homology is not clear in the sense of Article 6 PCT, because it is vague and indefinite (PCT Guidelines, 11.03.2004, Chapter 5.34); and, in contrast with the term "identity", cannot be quantified: a molecule is or not homologous to another molecule. The appropriate terminology is to refer to a percent of identity, as stated in the specification on page 9, lines 5-6.

B) Claim 19

B1) The subject-matter of **claim 19** is not clear in the sense of Article 6 PCT, because it is defined by the result to be achieved. Such a definition is generally not allowable, as clearly stated in the PCT Guidelines, 11.03.2004, Chapter 5.35, because it merely amounts to a statement of the underlying problem. Such a definition is only allowable if (1) there is no other information available in the application which could have enabled the applicant to define the product satisfactorily by reference to its composition, structure or some other parameters and (2) if the result can be directly and successfully checked, by the use of test and procedures clearly specified in the description and requiring nothing more than simple test. This is not the case in the present application, since one technical option, the 16S RNA DNA sequence, is disclosed within the dependent claims and the description.

B2) Moreover, the application has provided technical support for only a very limited number of ways of measuring the presence of the indicated bacteria - by measuring

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/IB2004/003310

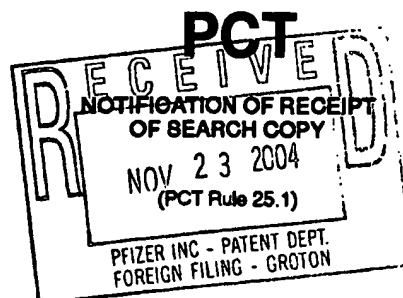
the presence of the corresponding 16S RNA DNA sequence - whereas the claims embrace all possible technical options of arriving at the desideratum. Consequently, the ISA considers that claim 19 does not meet the requirements of **Articles 5 and 6 PCT**, because it is insufficient to enable the skilled person to carry out the invention over the whole of the broad field claimed, without undue burden and without inventive skills.

U.G.

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

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UNITED STATES OF AMERICA



Date of mailing
 (day/month/year) **16/11/2004**

Applicant's or agent's file reference

PC25634A

IMPORTANT NOTIFICATION

International application No.

PCT/IB2004/003310

International filing date (day/month/year)

11/10/2004

Priority date (day/month/year)

23/10/2003

Applicant

PFIZER PRODUCTS INC.

1. Where the International Searching Authority and the receiving Office are not the same office:

The applicant is hereby notified that the search copy of the international application was received by this International Searching Authority on the date indicated below.

Where the International Searching Authority and the receiving Office are the same office:

The applicant is hereby notified that the search copy of the international application was received on the date indicated below.

26/10/2004 (date of receipt).

2. ☒ The search copy was accompanied by a nucleotide and/or amino acid sequence listing or tables related thereto in computer readable form.

3. Time limit for establishment of international search report and written opinion of the International Searching Authority

The applicant is informed that the time limit for establishing the international search report and the written opinion of the International Searching Authority is three months from the date of receipt indicated above or nine months from the priority date, whichever time limit expires later (Rules 42.1 and 43bis.1(a))

4. A copy of this notification has been sent to the International Bureau and, where the first sentence of paragraph 1 applies, to the receiving Office.

Name and mailing address of the International Searching Authority



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PATENT COOPERATION TREATY

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ACKNOWLEDGEMENT OF RECEIPT OF
DOCUMENTS FILED WITH THE
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Date of mailing (day/month/year) 29 October 2004 (29.10.2004)	Facsimile No.: +1 860 441 5082
Applicant's or agent's file reference PC25634A	IMPORTANT COMMUNICATION
International application No. PCT/IB2004/003310	International filing date (day/month/year) 11 October 2004 (11.10.2004)
Applicant PFIZER PRODUCTS INC. et al	
Title of the invention VACCINE FOR PERIODONTAL DISEASE	

1. The International Bureau has received the document/elements listed below on 28 October 2004 (28.10.2004) by the following means: delivery service

- ☒ PCT Request (1 page) (replacement sheet)
- ☐ description (excluding sequence listing part)
- ☐ claims
- ☐ abstract
- ☐ drawings
- ☐ sequence listing part of description
- ☐ fee calculation sheet
- ☐ separate authorization to charge deposit account
- ☐ cheque
- ☐ cash (in person only)
- ☐ power(s) of attorney
- ☐ statement(s) explaining lack of signature
- ☐ priority document
- ☐ separate indications concerning deposited micro-organism or other biological material
- ☐ sequence listing in computer readable form.
- ☐ statement accompanying diskette containing sequence in computer readable form
- ☒ accompanying letter 1
- ☐ form PCT/RO/198 (RO/IB)
- ☐ PCT-EASY diskette
- ☐ other (specify):

2. Additional observations (if necessary):

Name and mailing address of the receiving Office International Bureau of WIPO PCT Receiving Office Section 34, chemin des Colombettes, 1211 Geneva 20, Switzerland Facsimile No. (41-22) 910 06 10	Authorized officer Nadia Guigard Telephone No. (41-22) 338 83 24
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